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Several 3-azido-1,2,4-triazine 1-oxides were prepared by treating the appropriate 3-hydrazino derivatives with nitrous acid. 3-Azido-1,2,4-triazine 2-oxide was prepared by reaching the corresponding 3-bromo derivative with either tetramethylguanidinium azide in chloroform or sodium azide in aqueous acetone. The azido derivatives which could cyclize to form the tetrazolo isomers were proven to exist enitrely in the open chain form by a ^{13}C nmr, ^{1}H nmr and infrared spectroscopic study.

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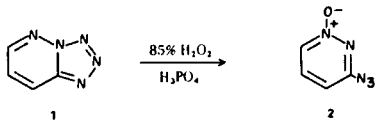
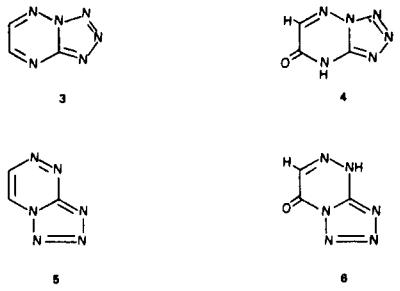
Many studies (1) have been performed to determine how electron donating and withdrawing substituents affect the tetrazolo-azido equilibrium in a number of tetrazoloazines. However, very little attention has been given to the effect that *N*-oxidation of the azine molecule might have on these equilibria. The only study reported on a monocyclic system is by Tisler and coworkers (2) who found that treatment of tetrazolo[1,5-*b*]pyridazine (1) with concentrated hydrogen peroxide in polyphosphoric acid led to direct *N*-oxidation of the pyridazine ring, and subsequent opening of the tetrazolo ring to afford 3-azidopyridazine 1-oxide (2).



1 2

Recently we have shown that 3-azido-1,2,4-triazines cyclize spontaneously to form tetrazolo[1,5-*b*]-1,2,4-triazines (3,4) rather than the isomeric compounds of type 5,6 and that when cyclization into N-2 is impossible as in



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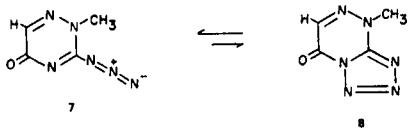
derivative 7, the indicated azido-tetrazolo equilibrium exists (3,4):



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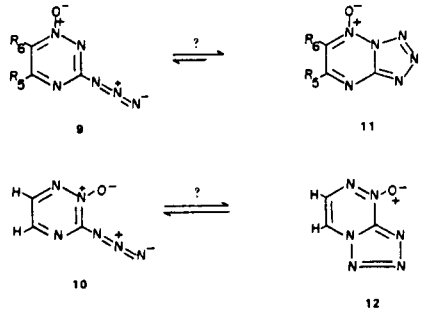
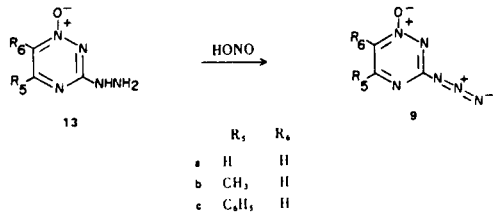
In view of our interest in 3-azido-1,2,4-triazines and the possibilities of different cyclizations we decided to study the behavior of some 3-azido-1,2,4-triazine 1- (9) and 2-oxides (10).



9 11 10 12

The desired 3-azido-1,2,4-triazine 1-oxides (*cf* Scheme I) were prepared by treatment of the appropriate 3-hydrazino-1,2,4-triazine 1-oxides with nitrous acid.

Scheme I



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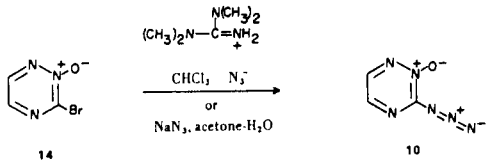
	R_5	R_6
a	H	H
b	CH_3	H
c	C_6H_5	H

3-Azido-1,2,4-triazine 2-oxide (10) was prepared by treatment of 3-bromo-1,2,4-triazine 2-oxide (14) (6) with either tetramethyl guanidinium azide in chloroform or with sodium azide in aqueous acetone.



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Infrared Spectral Data.

The nujol mull and chloroform solution infrared spectra of all of the compounds examined showed absorption bands in the azide region at 2150 cm^{-1} (see Table I). Since the infrared spectra of these compounds were devoid of absorption bands typical for tetrazolo [1,5-*b*]-1,2,4-triazines (1000-1100 cm^{-1}) it can be concluded that in the solid phase and in chloroform solution the azido form is the most stable.

Table I

Infrared Absorption Spectra (cm^{-1})

Compound No.	Phase	Azido bands
9a	Chloroform	2150 (s), 2200 (m)
	Nujol	2150 (s), 2200 (m)
9b	Chloroform	2150 (s)
	Nujol	2150 (s)
9c	Chloroform	2420 (s), 2450 (m)
	Nujol	2420 (s), 2450 (m)
10	Chloroform	2130 (s), 2150 (s)
	Nujol	2130 (s), 2160 (s)

Table II

^{1}H Nmr Spectra of Some 3-Azido-1,2,4-triazine *N*-Oxides (Chemical Shifts in δ)

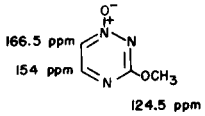
Compound No.	Solvent (a)	R_6	R_5	J_{AB}, Hz
9a	DMSO-D_6	8.38	8.80	4.0
	Deuterio-chloroform	7.90	8.50	4.5
9b	DMSO-D_6	8.40	2.47	
	Deuterio-chloroform	7.76	2.40	
9c	Deuterio-chloroform	8.34	8.10-8.00 (m) 7.62-7.54 (m)	
10	DMSO-D_6	8.58	8.21	3.0
	Deuterio-chloroform	8.31	7.97	3.0

(a) Dilute solutions in indicated solvent; see Scheme I for structure identifications. A Varian HA-100 spectrometer was used to obtain these spectra.

^{1}H and ^{13}C Nmr Spectral Data.

The ^{1}H nmr spectra in deuteriochloroform of all of the compounds examined showed the presence of only one isomer (see Table II). Thus, based upon the infrared data, which proved the existence of the azido rather than a bicyclic form in deuteriochloroform, the various proton chemical shifts can be assigned to the azido derivatives. The methyl group protons of the 3-azido-5-methyl derivative (**9b**) absorb at 2.40 δ and H-6 at 7.76 δ. The ^{1}H nmr spectrum of the parent 3-azido-1,2,4-triazine 1-oxide (**9a**) has only two protons (H-5, 8.50 δ and H-6, 7.90 δ) as an AB system (J_{AB} = 4.5 Hz). The ^{1}H nmr spectrum of the parent 3-azido-1,2,4-triazine 2-oxide (**10**) shows only two protons (H-5, 7.97 δ and H-6, 8.31 δ) as an AB system (J_{AB} = 3 Hz).

The ^{1}H nmr spectra in perdeuteriodimethyl sulfoxide of all of the compounds examined show the presence of only one "isomer". Unfortunately, the ring proton absorptions in deuteriochloroform and DMSO-D_6 are not the same. Thus, in order to determine which isomer we are dealing with in perdeuteriodimethyl sulfoxide we took recourse to a ^{13}C nmr spectral comparison of compounds **9a** and **10** with the recently described spectra of compounds **15** and **16** (6).



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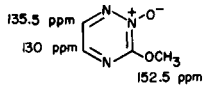

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3-Azido-1,2,4-triazine 1-oxide (**9a**) has 3 carbon signals at 167, 159.5 and 125 ppm, respectively. The carbon atom bearing the azido function at C-3 is expected to have the longest relaxation time (lowest intensity peak) and is readily identified as having a chemical shift of 167 ppm.

The two remaining peaks at 125 and 153.5 ppm, respectively, can be assigned in the following manner. The carbon atom *ortho* to the *N*-oxide function is expected to have a longer relaxation time (relative peak heights 3:7.5 for C-6 vs C-5 and is ascribed to the former while the most intense peak must be due to C-5.

In a similar manner the ^{13}C nmr chemical shifts of compound **10** (153, 131, and 136.0 ppm, respectively) were assigned to C-3, C-5 and C-6. Clearly, by comparing the ^{13}C resonances of the 3-azido-1,2,4-triazine *N*-oxides with the corresponding 3-methoxy-1,2,4-triazine *N*-oxides, it can be concluded that even in perdeuteriodimethyl sulfoxide the azido "isomer" is the most stable.

Thus, *N*-oxidation of 3-azido-1,2,4-triazines either at N-1 or N-2 sufficiently destabilizes the bicyclic compounds (**11**,**12**) to afford only the azido monocyclic compounds (**9**,**10**).

Table III

3-Azido-1,2,4-triazine *N*-Oxides

Molecular formula	Compound No.	M.p. °C	% Yield	Theory (%) C	H	N	Found (%) C	H	N
$C_3H_2N_6O$	**9a**	69-70	80	26.09	1.45	60.87	26.15	1.73	60.59
$C_4H_4N_6O$	**9b**	69-70.5	82	31.58	2.63	55.26	31.61	2.64	55.32
$C_9H_6N_6O$	**9c**	147.149	85	50.48	2.80	39.25	50.43	2.81	39.15
$C_3H_2N_6O$	**9d**		68 (a) (86) (b)	26.09	1.45	60.87	26.19	1.68	60.57

(a) Method A. (b) Method B.

EXPERIMENTAL

Preparation of 3-Azido-1,2,4-triazine 1-Oxides (**9a-c**).

General Procedure.

The appropriate 3-hydrazino-1,2,4-triazine 1-oxide (**13a-c**) (2 mmole) was dissolved in 5*N* hydrochloric acid (6 ml.). The solution was cooled to 0-5° and aqueous sodium nitrite (140 mg., 1 ml. of water) was added dropwise. The solution was stirred for an additional 15 minutes while maintaining the temperature at 0-5°. The crude tetrazole was separated either by filtration, (compound **9c**) or by extraction with chloroform (compounds **9a,b**). The compounds thus obtained were sublimed (50°/0.1 torr). (*cf.* Table III for analytical data.)

Preparation of 3-Azido-1,2,4-triazine 2-Oxide (**10**).

Method A.

3-Bromo-1,2,4-triazine 2-oxide (**14**) (880 mg., 5 mmoles) was dissolved in 250 ml. of chloroform. The solution was cooled to 0-5° and 800 mg. (6 mmoles) of tetramethylquanidinium azide was added. The solution was stirred for 8 hours and 70 ml. of anhydrous ether was added. The precipitated tetramethyl quanidinium bromide was filtered and the resulting solution was evaporated to dryness *in vacuo*. The residue thus obtained was sublimed (50°/0.1 torr).

Method B.

3-Bromo-1,2,4-triazine 2-oxide (14) (1.76 g., 0.01 mole) was dissolved in 20 ml. of acetone and sodium azide (650 mg.) dissolved in 5 ml. of water was added.

A precipitate immediately formed. The solution was heated to 50° and then cooled to room temperature. Twenty ml. of water was added and the resulting solution was extracted with methylene chloride (4 x 50 ml.). The extracts were dried (magnesium sulfate) and evaporated to dryness *in vacuo* to afford 1.18 g. of a yellow solid.

REFERENCES AND NOTES

(1) M. Tisler, *Synthesis*, 123 (1973).

(2) B. Stanovnik, M. Tisler, M. Ceglar, and U. Bah, *J. Org. Chem.*, 35, 1138 (1970).

(3) M. M. Goodman, J. Atwood, R. Carlin, W. Hunter, and W. W. Paudler, *ibid.*, 41, 2860 (1976).

(4) M. M. Goodman and W. W. Paudler, *ibid.*, in press (1977).

(5) W. W. Paudler and T. K. Chen, *ibid.*, 36, 787 (1971).

(6) R. J. Radel, B. T. Keen, C. Wong and W. W. Paudler, *ibid.*, 42, 546 (1977).